

CLAIMS

What is claimed is:

1. A method of diagnosing non-small cell lung cancer (NSCLC) in a human, the method comprising assessing expression of the gene encoding DAP-kinase in lung cells of the human, whereby a lower degree of expression of the gene in the human, relative to a normal level of expression of the gene in humans not afflicted with NSCLC, is an indication that the human is afflicted with NSCLC.

2. The method of claim 1, wherein expression of the gene is assessed in vitro in cells obtained from the human.

3. The method of claim 2, wherein the cells are obtained from a bronchial lavage.

4. The method of claim 2, wherein the cells are epithelial cells.

5. The method of claim 1, wherein the human does not exhibit a macroscopic clinical symptom of NSCLC.

6. The method of claim 5, wherein the symptom is selected from the group consisting of a cough that doesn't go away and gets worse over time, constant chest pain, coughing up blood, shortness of breath, wheezing, hoarseness, repeated problems with pneumonia, repeated problems with bronchitis, swelling of the neck and face, loss of appetite, weight loss, and fatigue.

7. The method of claim 1, wherein expression of the gene is assessed by assessing the methylation state of the gene.

8. The method of claim 7, wherein the methylation state of the gene is assessed by assessing the methylation state of the promoter CpG region of the gene.

9. The method of claim 7, wherein the methylation state of the gene is assessed using an oligonucleotide that specifically hybridizes with the methylated form of the gene.

5 10. The method of claim 9, wherein the oligonucleotide and a second oligonucleotide are used in a polymerase chain reaction (PCR) to amplify a portion of the gene.

11. A method of assessing NSCLC tumorigenesis at an early stage in a human, the method comprising assessing methylation of the gene encoding DAP-kinase in lung cells of
10 the human.

12. A method of assessing aggressiveness of a NSCLC tumor in a human, the method comprising assessing methylation of the gene encoding DAP-kinase in lung cells of the human, whereby a higher degree of methylation of the gene is an indication that the tumor is
15 more aggressive.

13. The method of claim 12, wherein the tumor is a diagnostic stage I NSCLC tumor.

20 14. A method of selecting among methods of treating a NSCLC tumor in a human, the method comprising assessing methylation of the gene encoding DAP-kinase in lung cells of the human and selecting a more aggressive treatment when a higher degree of methylation of the gene is detected.

25 15. A method of inhibiting NSCLC tumorigenesis in a human, the method comprising inhibiting methylation of the DAP-kinase gene in lung cells of the human.

16. A method of inhibiting progression of a NSCLC tumor in a human, the method comprising inhibiting methylation of the DAP-kinase gene in cells of the tumor.

17. A method of reducing the aggressiveness of a NSCLC tumor in a human, the method comprising inhibiting methylation of the DAP-kinase gene in cells of the tumor.

18. A method of inhibiting NSCLC tumorigenesis in a human, the method
5 comprising de-methylating the DAP-kinase gene in lung cells of the human.

19. A method of inhibiting progression of a NSCLC tumor in a human, the method comprising de-methylating the DAP-kinase gene in cells of the tumor.

20. A method of reducing the aggressiveness of a NSCLC tumor in a human, the method comprising de-methylating the DAP-kinase gene in cells of the tumor.

21. A method of assessing the risk that a human will develop NSCLC, the method comprising assessing expression of the gene encoding DAP-kinase in lung cells of the
15 human, whereby a lower degree of expression of the gene in the human, relative to a normal level of expression of the gene in humans not afflicted with NSCLC, is an indication that the human is at an increased risk for developing NSCLC.

22. A method of assessing whether a test compound is useful for inhibiting a
20 process selected from the group consisting of i) NSCLC tumorigenesis, ii) progression of a NSCLC tumor, and iii) aggressiveness of a NSCLC tumor, the method comprising comparing methylation of the DAP-kinase gene in the presence of the test compound and methylation of the gene in the absence of the test compound, whereby a lower degree of gene methylation in the presence of the test compound is an indication that the test compound is useful for
25 inhibiting the process.

23. A method of preventing NSCLC in a human at risk for developing NSCLC, the method comprising inhibiting methylation of the DAP-kinase gene in lung cells of the human.

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24. A method of preventing NSCLC in a human at risk for developing NSCLC, the method comprising enhancing de-methylation of the DAP-kinase gene in lung cells of the human.

5 25. A method of alleviating NSCLC in a human, the method comprising inhibiting methylation of the DAP-kinase gene in lung cells of the human.

26. A method of alleviating NSCLC in a human, the method comprising enhancing de-methylation of the DAP-kinase gene in lung cells of the human.

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27. A method of diagnosing NSCLC in a human, the method comprising assessing expression of the HOXA9 gene in lung cells of the human, whereby a greater degree of expression of the gene in the human, relative to a normal level of expression of the gene in humans not afflicted with NSCLC, is an indication that the human is afflicted with NSCLC.

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28. The method of claim 27, wherein expression of the gene is assessed in vitro in cells obtained from the human.

29. The method of claim 28, wherein the cells are obtained from a bronchial lavage.

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30. The method of claim 28, wherein the cells are epithelial cells.

31. The method of claim 27, wherein the human does not exhibit a macroscopic clinical symptom of NSCLC.

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32. The method of claim 31, wherein the symptom is selected from the group consisting of a cough that doesn't go away and gets worse over time, constant chest pain, coughing up blood, shortness of breath, wheezing, hoarseness, repeated problems with

pneumonia, repeated problems with bronchitis, swelling of the neck and face, loss of appetite, weight loss, and fatigue.

33. The method of claim 27, wherein expression of the gene is assessed using an
5 oligonucleotide that specifically hybridizes with a transcription product of the gene.

34. The method of claim 33, wherein the oligonucleotide does not specifically
hybridize with the gene.

10 35. The method of claim 33, wherein the oligonucleotide and a second
oligonucleotide are used in a polymerase chain reaction (PCR) to amplify a portion of the gene.

36. The method of claim 35, wherein the portion includes sub-portions wherein
an intron is interposed between the sub-portions in the gene, but wherein the sub-portions are
15 adjacent in mRNA derived from the gene.

37. A method of assessing the risk that a human will develop NSCLC, the
method comprising assessing expression of the HOXA9 gene in lung cells of the human,
whereby a greater degree of expression of the gene in the human, relative to a normal level of
20 expression of the gene in humans not afflicted with NSCLC, is an indication that the human is
at an increased risk for developing NSCLC.

38. A method of inhibiting NSCLC tumorigenesis in a human, the method
comprising inhibiting expression of the HOXA9 gene in lung cells of the human.
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39. A method of inhibiting progression of a NSCLC tumor in a human, the
method comprising inhibiting expression of the HOXA9 gene in cells of the tumor.

40. A method of assessing whether a test compound is useful for inhibiting a
30 process selected from the group consisting of i) NSCLC tumorigenesis and ii) progression of a

NSCLC tumor, the method comprising comparing expression of the HOXA9 gene in the presence of the test compound and expression of the gene in the absence of the test compound, whereby a lower degree of expression in the presence of the test compound is an indication that the test compound is useful for inhibiting the process.

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41. A method of preventing NSCLC in a human at risk for developing NSCLC, the method comprising inhibiting expression of the HOXA9 gene in lung cells of the human.

42. A method of alleviating NSCLC in a human, the method comprising
10 inhibiting expression of the HOXA9 gene in lung cells of the human.